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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/765,555	01/19/2001	Carlos F. Barbas III	278012001420	1190

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EXAMINER

IBRAHIM, MEDINA AHMED

ART UNIT PAPER NUMBER

1638

DATE MAILED: 02/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/765,555

Applicant(s)

BARBAS ET AL.

Examiner

Medina A Ibrahim

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 December 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) See Continuation Sheet is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) See Continuation Sheet is/are rejected.
- 7) ☒ Claim(s) 139 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Continuation of Disposition of Claims: Claims pending in the application are 1,4-8,11,13-16,18-22,28-30,36-44,46,48,50-59,61-66,70-72,74,76-78,83,85,88,91-95,98-100,133-137 and 139.

Continuation of Disposition of Claims: Claims rejected are 1,4-8,11,13-16,18-22,28-30,36-44,46,48,50-59,61-66,70-72,74,76-78,83,85,88,91-95,98-100 and 133-137.

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DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant's response filed 12/10/04 in reply to the Office action of 09/10/04 has been entered. Claims 1, 4, 8, 11, 13, 28-30, 39, 42, 48, 52-55, 58, 64-65, 70, 74, 76, 83, 85, 88, 93, 95, 99-100 are currently amended. Claims 3, 31, 60, 69, 73, 79-82, 84, 97 have been cancelled. Claim 139 have been added. Therefore, claims 1, 4-8, 11, 13-16, 18-22, 28-30, 36-44, 46, 48, 50-59, 61-66, 70-72, 74, 76-78, 83, 85, 88, 91-95, 98-100, 133-137, and 139 are pending and are under consideration.

All previous rejections and objections not set forth below have been withdrawn in view of Applicant's amendment to the claims.

Sequence Listing

Applicant's CRF and paper sequence listings filed 12/10/04 have been entered. However, this application fails to comply with the requirements of 37 CFR 1.821-1.825 because sequences of the sequence listings (Paper and CRF) do not match those listed on Figure 24. For example, SEQ ID NO: 1 has 532 bp in the sequence listings, but has 531 bp in Fig. 24. SEQ ID NO: 4 is 3121 bp long in the sequence listings, but 3120 bp in the figure. SEQ ID NO: 6 has 156 bp in the sequence listings, but 155 bp in the figure. Applicant has neither corrected the sequences, nor has provided reason why the sequences in the sequence listings differ from those on Figure 24.

Claim Objections

Claim 139 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112

Claims 1, 4-8, 11, 13-16, 8-22, 28-30, 36-44, 46, 48, 50- 59, 61-66, and 133-137 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of modulating the expression level of a target gene in a plant /plant cell by transforming the plant/ cell with a nucleotide sequence encoding a synthetic zinc finger proteins that are designed to target unique sequences of the formula (GNN) 6, or a nucleotide sequence containing 18 consecutive nucleotides with GNN and TGA triplets; an expression vector comprising a nucleic acid encoding the synthetic zinc finger proteins of SEQ ID NO: 38, 39, 40, 41 or 42, transgenic plants/cells/seed comprising said expression vector, does not reasonably provide enablement for any method to modulate the expression of a target gene with a zinc finger protein capable of binding to any 18 nucleotides within the target gene. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. This rejection is repeated for the reasons set forth in the Office action of 09/10/04. Applicant's arguments filed 12/10/04 have been considered but are not deemed persuasive.

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Applicant asserts that the teachings of the specification on page 28, line 17 to page 30, line 22, provide sufficient guidance to those of ordinary skill in the art to practice the full scope of the claims without undue experimentation. Applicant argues that Choo and Isalan et al (2000) reference is not limited to producing fingers that bind particular subsets of DNA sequences, but that it also teaches the possibility to target any sequence of interest using their method (response, p. 15).

This is not persuasive because claims drawn to a method for stably modulating the expression of a target gene in a plant/cell by using a synthetic zinc finger protein that binds to any 18 nucleotides within a target gene or complementary strand thereof, and stably transformed plant, plant cells and seed with modulated target gene are not supported by an enabling disclosure, as discussed in the last Office actions of 05/21/03 and 09/10/04. Neither the instant specification nor the prior art teaches obtaining synthetic zinc finger proteins that are capable of targeting any non-contiguous 18 nucleotides within the target gene, thereby modulating the expression level of the target gene. On pages 28-30 of the specification, Applicant teaches designing zinc finger protein domains with triplet/quadruplet recognition code. On page 31 of the specification, Applicant discusses designing a ZFP to bind non-contiguous target sequences separated by intervening sequences. For example, the specification suggests designing a six-finger zinc finger protein that binds to 2 nine base pairs separated by intervening bases. However, the instant claims are not limited to the use of such ZFPs.

Regarding Choo et al (2000), it is noted that the reference not only teaches the

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limitations of designing zinc finger polymers that bind to DNA in which every third base is not guanine or thymine, but also teaches the limitation of designing ZFPs that recognize a greater diversity of nucleotide sequences (see paragraph bridging columns 411 and 412; the last two sentences of the paragraph bridging pages 412 and 413). On page 414, column 2, 1st full paragraph, Choo et al also discussed about the prospects of using designed zinc finger proteins for gene regulation. Choo et al state, "Our experience is that each of these methods can be effective, however, the magnitude of the effect depends on the particular system that is studied". Therefore, Choo et al reference does not appear to support the use of synthetic zinc finger binding proteins to target any 18 nucleotides within a target gene in a transgenic plant, without having to engage in undue experimentation.

See *Genentech Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1366, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997) where it states [It] is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement". The *Genentech* court also held that [w]hile every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention". *Id.* In this case, as in *Genentech*, the specification does not provide the "reasonable detailto enable members of the public to understand and carry out the invention".

Therefore, given the breadth of the claims; the limited guidance in the specification; the state of the art, and the unpredictability inherent in gene regulation in

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transgenic plants as discussed in the last Office actions of 05/21/03 and 09/10/04, the claimed invention is not enabled throughout the broad scope.

Remarks

The claims are deemed free of the prior art because the prior art does not teach or fairly suggest a method to stably modulate the expression level of a target gene in a transgenic plant using synthetic zinc finger proteins that targets 18 nucleotides within the target gene; nor that the prior art teaches an expression vector comprising ZFPm1, ZFPm2, ZFPm3, ZFPm4 or ZFPAp3.

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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Contact information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Medina A. Ibrahim whose telephone number is (571) 272-0797. The Examiner can normally be reached Monday -Thursday from 8:00AM to 5:30PM and every other Friday from 9:00AM to 5:00 PM . Before and after final responses should be directed to fax nos. (703) 872-9306 and (703) 872-9307, respectively.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Amy Nelson, can be reached at (571) 272-0804.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

2/15/05

Mai

A handwritten signature in black ink, appearing to read "Amy Nelson", is positioned to the right of the date and name.

AMY J. NELSON, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600